

Immunology and the Jeffrey Modell Foundation

A 2019 Update

How our understanding of the immune system is now offering remarkable opportunities for conquering diseases...

I. Why Immunology?

For more than 30 years the Jeffrey Modell Foundation has focused its efforts on the immune system because it holds the key to conquering so many diseases that have plagued humankind.

Millions of people around the world die needlessly from conditions that could be cured or prevented if the immune system functioned normally. **Infectious diseases alone kill more people than any other single cause. The failure of the immune system to function properly, contributes to two-thirds of the deaths of all Americans who die from infections each year.**

Simply put, harnessing the power of the immune system represents one of the single greatest disease-fighting, and life-saving strategies that biomedical science has to offer. The best medicine lies within us!

II. What we know:

1. How the Immune System Works

Each day, our bodies are under attack. While invisible to the naked eye, millions of bacteria, viruses and other microorganisms constantly circulate around us. Our immune system protects us via a network of more than a trillion cells, working together in tissues and organs to create our very own department of defense. Basically, it is our immune system's job to keep foreign invaders out or, failing that, to destroy them once they enter our bodies. This process works most of the time, although not always, which is why we occasionally struggle in recovering quickly from colds, flu, and other infections.

2. Infectious Diseases and Vaccines

An encounter with a virus "teaches" the immune system to recognize and remember that viral "bad guy" in the future. This "immune memory" is a hallmark of the immune system that enables it to wipe out that same virus with breakneck speed, if seen again. A vaccine's purpose is to create immune memory, conferring protection without an individual ever having to be infected with the pathogen as it exists in nature. To accomplish this, vaccines usually contain noninfectious pieces of viruses or bacteria that trigger the immune response, cementing the immune system's memory, without causing sickness. Upon encountering the actual live virus, the immune system uses antibodies and "killer" cells, which act like a team of cellular ninjas seeking out and destroying the previously encountered invaders.

3. Autoimmune Diseases

The key feature of a healthy immune system is its remarkable ability to distinguish between cells in the human body and foreign cells. When immune defense cells encounter these foreign invaders (i.e., viruses, bacteria), they quickly launch an attack. Unfortunately, in an apparent case of mistaken identity, individual immune systems sometimes get it wrong and attack healthy cells and/or tissues. This results in damage leading to autoimmune diseases, such as Type 1 Diabetes, Rheumatoid Arthritis, Inflammatory Bowel Disease, and Multiple Sclerosis.

4. Inflammatory Diseases

Inflammation is the gathering of immune system cells and molecules at an infected or injured site. This immune response is good for the body, and is designed to promote healing. The clearest example of this

process at work can be viewed when an individual cuts his or her finger. The initial swelling and redness (inflammation) indicates that the immune system is busily working to heal the cut. However, trouble arises when this inflammatory response is prolonged or shows up where it is not needed. In prolonged instances, inflammation harms body tissues. Heart Disease, Type 2 Diabetes, Stroke and many other diseases are linked to chronic inflammation.

5. Immunotherapy

Today, researchers and clinicians are very actively using the Immune System at the molecular level as the engine to attack disorders, including cancers. Immunotherapy offers us a chance to create treatments and potential cures. Researchers, now with a greater understanding of what controls T-cells, have an excellent chance to understand how T-cells can be modulated to attack a number of different disorders.

III. New Developments in Gene Editing, CRISPR-Cas9, and RNA Technology

1. Today there is new technology for editing genes. Precise edits to DNA strands in the cells using little bits of DNA can trigger a tiny but critical change in a single gene.
2. Many bacteria have an adaptive immune system in their cells called **CRISPR**. The CRISPR locus allows these cells to detect viral DNA and destroy the virus.
3. **Cas9** is a protein that is able to seek out, cut like a pair of scissors, and degrade viral DNA.
4. Here's how it works: When viruses infect a cell, viruses inject their DNA. In a bacterium, CRISPR allows DNA to be "plucked out" of the virus and inserted into chromosomes...the DNA of the bacterium. The viral DNA gets inserted at a site called CRISPR...clustered regularly interspaced short palindromic repeats.
5. CRISPR-Cas9 is RNA technology to manipulate gene expression by directly altering DNA.
6. **RNA** is the chemical cousin of DNA in our genes, and is a molecule that is an exact replication of viral DNA.
7. RNA interference is a powerful tool for shutting down individual genes to discover their function.
8. When we are able to program CRISPR technology to make a break in DNA near a mutation causing Severe Combined Immunodeficiency (SCID) for example, we could trigger cells to repair that mutation.

IV. What is the Future?

1. Today, with whole genome and targeted exome sequencing, gene editing, CRISPR-Cas9, RNA and other emerging technologies to analyze single cells, scientists have characterized our opportunities as extraordinary and breathtaking.
2. CRISPR and RNA are therapeutic tools to inactivate specific genes and disrupt genetic triggers of disease.
3. Immunotherapy including T-cell modulation, therapeutic vaccines, and monoclonal antibodies are at the leading edge of important scientific progress.
4. This technology can provide defense and interference against foreign invaders, resulting in a stronger healthier immune system.

5. We can now survey the human genome with unprecedented speed and precision. Transformative research will allow us to personalize prevention, diagnosis and treatment, improve human health, and finally cure human disease.
6. We can look to a future where we can address immune dysregulation, dysfunction and immunological inadequacies, at the cellular level, and immune modifying agents can contribute to controlling or preventing a wide spectrum of diseases.
7. Think of it. We can pinpoint the exact gene that causes the disease. In a growing number of cases, we can modify gene expression and actually stop a disease from occurring.

This is our time! This is our opportunity! Let us seize this moment.

V. The Jeffrey Modell Centers Network

1. The Jeffrey Modell Foundation has formed strong ties with major academic institutions and medical centers by establishing a global Jeffrey Modell Centers Network,
2. This network includes 821 physicians at 376 academic institutions, in 294 cities, 86 countries, spanning 6 continents and is growing.
3. 188,000+ patients have been identified and followed at our Centers.
4. Hundreds of new genes have been discovered and defined at Jeffrey Modell Centers and these discoveries have had an impact upon current and future therapies.
5. The Network collaboration has generated pioneering science and discovery, inspiring “out of the box thinking” and creativity resulting in life saving innovations. Manuscripts published by our Center Directors are among the most cited in Immunology.